

and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

***Amendment***

***In the Specification***

Please substitute the first paragraph at page 3 with the following paragraph:

It has been assumed that the functional Type I IL-1R is a single chain receptor (Curtis, B.M., *et al.*, *Proc. Natl. Acad. Sci. USA*, 86:3045-3049 (1989)). However, affinity cross-linking of IL-1 to cells expressing natural IL-1 receptor has yielded complex patterns of cross-linked proteins (Dower, *et al.*, *Cellular and Molecular Mechanisms of Inflammation*, pp. 137-172, Academic Press, Orlando FL (1990); Dinarello, *et al.*, *Immunol. Today*, 10: 49-51 (1989)). These cross-linking studies detect molecular mass complexes consistent with both the Type I and Type II IL-1Rs cross-linked to IL-1. In addition, in some studies, higher molecular mass complexes (>200 kD) are apparent (Kupper, T.S., *et al.*, *J. Clin. Invest.* 82:1787-1792 (1988); Dinarello, C.A., *et al.*, *Immunol. Today* 10:49-51 (1989); Solari, R., *Cytokine* 2:21-28 (1990); Mancilla, J., *et al.*, *Lymph. Cytokine Res.* 11:197-205 (1992)). Some reports have interpreted these higher molecular mass complexes to be dimers of receptor-ligand complexes. Others have concluded that these high molecular mass complexes maybe indicative of a multi-subunit IL-1 receptor complex.

Please substitute the paragraph beginning on page 5, line 11, with the following paragraph:

The present invention provides isolated nucleic acid molecules comprising a polynucleotide encoding the soluble IL-1R AcM polypeptide having the amino acid sequence as shown in Figure 1 (SEQ ID NO:2) or the amino acid sequence encoded by the cDNA clone deposited as ATCC Deposit Number 97666 on July 25, 1996. The nucleotide sequence determined by sequencing the deposited IL-1R AcM clone, which is shown in Figure 1 (SEQ ID NO:1), contains an open reading frame encoding a polypeptide of 356 amino acid residues, including an initiation codon at positions 303-305, with a leader sequence of about 17 amino acid residues, and a predicted molecular weight of about 42 kDa. The amino acid sequence of the mature IL-1R AcM protein is amino acid residues 18-356 shown in Figure 1 or 1-339 shown in SEQ ID NO:2.

C<sup>2</sup>

Please substitute the paragraph beginning on page 9, line 7, with the following paragraph:

The present invention also provides the mature form(s) of the soluble IL-1R AcM protein of the present invention. According to the signal hypothesis, proteins secreted by mammalian cells have a signal or secretory leader sequence which is cleaved from the mature protein once export of the growing protein chain across the rough endoplasmic reticulum has been initiated. Most mammalian cells and even insect cells cleave secreted proteins with the same specificity. However, in some cases, cleavage of a secreted protein

C<sup>3</sup>

is not entirely uniform, which results in two or more mature species on the protein. Further, it has long been known that the cleavage specificity of a secreted protein is ultimately determined by the primary structure of the complete protein, that is, it is inherent in the amino acid sequence of the polypeptide. Therefore, the present invention provides a nucleotide sequence encoding the mature soluble IL-1R AcM polypeptides having the amino acid sequence encoded by the cDNA clone identified as ATCC Deposit No. 97666 and as shown in SEQ ID NO:2. By the mature soluble IL-1R AcM protein having the amino acid sequence encoded by the cDNA clone identified as ATCC Deposit 97666 is meant the mature form(s) of the soluble IL-1R AcM protein produced by expression in a mammalian cell (e.g., COS cells, as described below) of the complete open reading frame encoded by the human DNA sequence of the clone contained in the vector. As indicated below, the mature soluble IL-1R AcM having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97666 may or may not differ from the predicted "mature" soluble IL-1R AcM protein shown in SEQ ID NO:2 (amino acids from about 1 to about 339) depending on the accuracy of the predicted cleavage site based on computer analysis.

C<sup>3</sup>  
Cont